REMARKS

With this response, claims 50 and 54-58 have been amended; claims 42-43, 45, 47-49, 51, 53, 59, 62, 65, 68, 71, 74, 77, and 80 have been canceled, without prejudice or disclaimer; and new claims 83-90 have been added. Thus, upon entry of the present response, claims 44, 46, 50, 52, 54-58, 60-61, 63-64, 66-67, 69-70, 72-73, 75-76, 78-79, and 81-90 will be pending.

Since the Office Action of November 18, 2003 indicated claims 60-61, 63-64, 66-67, 69-70, 72-73, 75-76, 78-79, and 81-82 as allowable[1], it is believed that claims 44, 46, 50, 52, 54-58, and 83-90 are currently under examination.

Claim 50 has been amended to specify the MR1 antibody produced by the recited hybridoma, and to conform with the claim language of claim 52.

Claims 54-58 have been amended so as to not depend from a canceled claim, and in matters of formal claim language.

New claims 83-90 are directed to a method of inhibiting immunoglobulin production or activation of B-cells comprising contacting T-cells with, or administering to an animal, an effective amount of an antibody that that binds an antigen that is present on activated but not resting T-cells, has the same molecular weight as a protein precipitated by CD40-Ig fusion protein, and is pre-cleared by precipitation with the CD40-Ig; wherein the antibody blocks binding of the CD40-Ig to activated T-cells and inhibits T-cell induction of B-cell activation. This is fully supported by the original specification at, *e.g.*, page 11, lines 25-35; page 14, lines 6-13 (Figure 5b) and 19-27 (Figure 1b and 6); page 15, lines 15-17 (and Figure 3); page 17, lines 13-18; page 22, lines 25-35 (Figure 8); and page 26, line 15 to page 28, line 30 (Figure 4); and page 29, line 4 to page 30, line 35.

[1] The Office Action actually indicated claims 60-61, 63-64, 66-67, 69-70, 72-73, 75, 77-79, and 81-82, as allowable. However, after a review of the Examiner's reasoning in the office action and its rejections, the undersigned believe that the Examiner actually intended to allow claim 76 instead of claim 77. If this is incorrect, and claim 77 is allowed while claim 76 is rejected, the Examiner is respectfully requested to contact the undersigned.

No new matter has been added by way of this amendment. Each of the Examiner's rejections are discussed below.

Substitute Specification

With Applicant's response of June 9, 2003, a mark-up version of a substitute specification was enclosed, and the Examiner requested that a clean copy of the specification be submitted as well.

With this response, a new substitute specification, in the form of both a mark-up version and a clean copy of the mark-up version per 37 C.F.R. 1.125(b) and (c) is submitted. This is done because errors were discovered in the mark-up version of the substitute specification submitted on June 9, 2003. It is respectfully requested that the presently submitted substitute specification (mark-up copy and clean copy) be used instead of the marked-up version of a substitute specification submitted on June 9, 2003.

In the mark-up version, added text is marked by double-underlining instead of single-underlining, since the original specification contained single-underlined text.

Per 37 C.F.R. 1.125(b)(1), it is hereby stated that the substitute specification accompanying this response contains no new matter.

New Matter

Claims 42, 43, 48, 49, 59, 62, 65, 68, 71, 74, 76, 80, and claims dependent therefrom, have been rejected as allegedly containing new matter.

With this rejection, claims 42, 43, 48, 49, 59, 62, 65, 68, 71, 74, 76, 80 have been canceled, without prejudice, and claims 54-58 depend from claims not included in this rejection. It is therefore believed that this rejection has been rendered moot, and should be withdrawn.

Written Description

Claims 43, 47, 49, 51, and claims dependent therefrom (claims 54-58) have been rejected as allegedly not complying with the written description requirement.

With this response, claims 43, 47, 49, and 51 have been canceled, without prejudice, and claims 54-58 depend from claims not included in this rejection. It is therefore believed that the rejection, as pertaining to these claims, has been rendered moot, and should be withdrawn.

New claims 83-90 call for an antibody binding to an antigen that (a) is present on activated but not resting T-cells; (b) has the same molecular weight as a protein precipitated by a CD40-immunoglobulin (CD40-Ig) fusion protein comprising the extracellular domain of a CD40 protein having the amino acid sequence of SEQ ID NO:2 and an extracellular domain at the site of fusion having the amino acid sequence of SEQ ID NO:3; and (c) is pre-cleared by precipitation with the CD40-Ig; which antibody blocks binding of the CD40-Ig to activated T-cells and T-cell induction of B-cell activation. Accordingly, in the present claims, the antigen is characterized by physical characteristics, cell distribution characteristic, ligand-binding characteristics, and the antibody is characterized by antigen-binding and functional characteristics, as discussed below.

Antigen Physical Characteristics: The antigen has the same molecular weight as a protein bound by Applicant's novel CD40-Ig construct, which has a ligand-binding domain fully characterized by amino acid sequence (SEQ ID NO:2). The antigen CD40-ligand, is a member of specific ligand-ligand pairs, and can be isolated and tested for molecular weight using methods identical to those employed in Example 1, page 28, lines 8-30 (Figure 4) and page 29, lines 13-17 (Figure 5b). Starting materials for the antigen can be cell membranes from activated helper T cells, prepared as described on page 21, lines 20-35; or as described in Example 2 (page 31, lines 20-31). As described on page 29, lines 16-17 and in figure 5b, using plasma membranes from murine helper T-cells, antibody MR1 and CD40-Ig both recognized a 39 kD protein.

Antigen Cell Distribution Characteristics: As described in Example 1, page 28, lines 8-30, the antigen is expressed on activated but not resting helper T-cells. This was shown in a binding

assay where activated helper T-cells stained 56% positive with CD40-Ig but not with the control construct CD7E-Ig (*Id.*). In addition, as described on page 29, lines 2-4, MR1 recognized an antigen that was selectively expressed on activated murine helper T- cells.

Antigen Ligand-Binding Characteristics: The antigen is pre-cleared by precipitation with CD40-Ig. See page 29, lines 18-22. This shows that the antigen is a member of a specific CD40 ligand-ligand binding pair.

Antibody Antigen-Binding Characteristics: The antibody blocks the specific binding of CD40-Ig to activated helper T-cells, showing that the antibody and CD40 have overlapping or identical binding epitopes on the antigen (page 29, lines 8-13). This is a unique characteristics of the claimed antibody.

Functional Characteristics: The antibody has the functional characteristic of inhibiting T-cell activation of B-cells. This is supported by, *e.g.*, Example 1, page 28, line 35 to page 29, line 30, of the original specification, where it is shown that MR1 antibody blocked B-cell activation while control antibodies did not.

It is noted that both in the present application (see, *e.g.*, claim 44) and in patents cited by the Examiner (see Lederman et al., U.S. Patent No. 5,993,816), claiming antibodies by virtue of their binding to an antigen specifically recognized or bound by a defined ligand is deemed by the Patent Office to comply with the written description requirement. As noted above, the ligand-binding portion of the CD40-Ig construct has a defined amino acid sequence as recited in new claims 83-90.

Additionally, in both paper Nos. 6 and 8 of the present prosecution file, dated November 19, 2001 and March 23, 2001, the Examiner stated that all claims were allowable. It is still not clear why the Examiner twice found the claims allowable, and then retracted his position to issue the present rejection.

In fact, the Federal Circuit has established that the specification of related application 08/742,480, filed November 1, 1996, provides adequate written description of antibodies to murine CD40L (see accompanying IDS reference No. CF at, e.g., page 3, 1st column, last paragraph). Since the specification of the present application was filed as a continuation of the 08/742,480 application, having an identical specification, it is respectfully submitted that the disclosed methods of using such antibodies also comply with the written description requirement.

For all of the above reasons, it is clear that the specification adequately supports the claims. Reconsideration and withdrawal of this rejection is therefore earnestly requested.

Anticipation

The Examiner has rejected claims 43, 45, 47, 49, 51, and 53-58 as allegedly anticipated by Lederman (U.S. Patent No. 5,993,816, "Lederman patent") under 35 U.S.C. §102(e).

This rejection is respectfully traversed based on applicant's previous request for interference under 37 C.F.R. §§ 1.607 and 1.608(a), submitted with the preliminary amendment filed December 20, 1999. Pursuant to the MPEP, section 2308.01 (emphasis added):

> If an applicant is claiming the same invention as a patent which has an earlier effective United States filing date but there is not a statutory bar against the application, and the applicant has not submitted the items required by 37 CFR 1.608(a) or (b), as appropriate, the application should be rejected under 35 U.S.C. 102(e)/ 103.

In the instant case, however, applicant has provided a statement under 37 C.F.R. § 1.608(a). Rejection under 35 U.S.C. 102(e) is therefore improper, and this rejection should be withdrawn.

Further, with this response, claims 43, 45, 47, 49, 51, and 53 have been canceled, without prejudice, and claims 54-58 depend from claims not included in this rejection. It is thereby believed that the rejection as applied to these claims is moot.

Obviousness

Claims 42-58 have been rejected as allegedly obvious under 35 U.S.C. §103 over the Lederman patent in view of Armitage (U.S. Patent No. 5,961,974, "Armitage patent"). Additionally, claims 42-58 have been rejected as allegedly obvious over the Lederman patent, or, in the alternative, the Lederman patent in view of the Armitage patent and Ultee (U.S. Patent No. 4,937,183; "Ultee patent").

As above, this rejection is respectfully traversed based on applicant's previous request for interference with the Lederman patent under 37 C.F.R. §§ 1.607 and 1.608(a), submitted with the preliminary amendment filed December 20, 1999. In addition, claims 42-43, 45, 47-49, 51 and 53 have been canceled, without prejudice. The Lederman patent is therefore not available as prior art against any claim of the present application, and, for this reason alone, the present rejections under 35 U.S.C. § 103 are moot and should be withdrawn.

It is noted, however, that neither the Armitage patent, nor its priority applications U.S. Serial Nos. 07/783,707, filed October 25, 1991, or 07/805,723 filed December 5, 1991, describe or suggest the use of antibodies against gp39 (CD40L) for inhibiting B-cell activation or immunoglobulin production by contacting T-cells with such antibodies. With respect to the Ultee patent, this reference does not describe anti-gp39 antibodies, CD40, or CD40-Ig, nor methods to inhibit B-cell activation or immunoglobulin production using such antibodies or any other antibodies. Furthermore, the Lederman patent does not teach or suggest an antibody specific for the antigen as recited in new claims 83-90 (see, *e.g.*, paragraphs (a) to (c) of claim 83).

Accordingly, since the Lederman patent is not available as prior art against the present claims, and since neither of the Armitage or Ultee patents, nor the combination thereof, describes or suggests the use of anti-gp39 antibodies for inhibiting B-cell activation or immunoglobulin production, the present claims are non-obvious. Reconsideration and withdrawal of this rejection is therefore requested.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to issue a statement to that effect and to promptly initiate interference proceedings.

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Respectfully submitted,

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